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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,036	07/30/2001	Kiran Madura	266/165	1466
34055	7590	06/17/2005	EXAMINER	
PERKINS COIE LLP POST OFFICE BOX 1208 SEATTLE, WA 98111-1208			WALICKA, MALGORZATA A	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 06/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/918,036

Applicant(s)

MADURA, KIRAN

Examiner

Malgorzata A. Walicka

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 24 May 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 6, 9, 10 and 12 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 6, 9, 10, and 12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application May 24, 2005, after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

Claims 1-5, 8, 11, and 13-18 were previously cancelled; claims 6 and 10 have been currently amended. Claims 6,7, 9,10 and 12 are pending and under examination.

### **DETAILED OFFICE ACTION**

#### **1. Rejections**

##### ***1.1. 35 USC, section 112, first paragraph***

###### ***1.1.1. Lack of written description***

Rejection of claims 6, 7, 9, 10 and 12 for lack of description of assessing the rate of proliferation a cell, made in the final rejection of November 26, 2005 and reiterated in the advisory action of March 15 2005, is withdrawn, because the amended claims do not recite "the rate of proliferation".

Claims 6, 7, 9, 10 and 12 are rejected for lack of written description of the term description "functional 26S proteasome". There is no term "functional 26S proteasome" in the disclosure. There is also nothing to suggest in the specification, or the claims as originally filed, that Applicants limit their method to the cells with a functional 26S proteasome. Introducing this limitation to the claims means introducing a new matter. Thus, the claims are rejected because they contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Furthermore, the claims are directed to a product, a DNA construct for assessing whether any cell with any functional 26S proteasome is quiescent or actively growing, as well as a method of its use. The term "functional 26S proteasome" is generic. Applicant describe on page 2, line 30 and further, and on page 3, line 12 and further, the structure of 26S proteasome as an extremely complex structure. It

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consists of two subcomplexes, a catalytical one of 20S and a regulatory one of 19S. In line 20 on page 3

Applicants inform,

"The 19S complex contains as many as 20 subunits, which include a multiubiquitin-chain binding protein, isopeptidases and at least 6 ATPases. To date, many of these additional subunits remain uncharacterized."

On page 37, line 3 and further, Applicants teach that cim5 ATPase is a component of 19S regulatory complex and that Rad23-HA is stable in exponentially growing *S. cerevisiae* cell carrying mutation in cim5. Also, when pre1 and pre2 subunits of the 20S catalytic core of the S26 proteasome are mutated, the exponentially growing mutants do not degrade Rad23-HA. The three examples of "nonfunctionality" of S26 proteasome, i.e., mutations in cim5, pre1 and pre2, are not representative of all possible mutations in components of the S26 proteome that make it nonfunctional, and, the relation of these other mutations to degradation of Rad 23-HA, or any other recited sequences of Ubl domains, are not disclosed. What more important, Applicants' data clearly suggests that the constructs containing Ubl domains can be used for testing whether a cell possesses a functional 26S proteasome, because when the 26S is not functional the chimeric protein is not degraded. Applicants' data does not show that active growth is correlated with rapid degradation of the Ubl containing proteins, because there are too many examples when active growth is accompanied by lack of degradation of the Ubl containing proteins; see also the discussion in the advisory action.

In conclusion, because the Applicants did not reasonably convey to one skilled in the relevant art that at the time the application was filed they had possession of the claimed invention, the claims are rejected.

#### 1.2.2. Scope of enablement

Claim 6-7 and 9, 10 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for degradation of Rad23<sup>1-369</sup>, Rad23-HA and Ubl<sup>R23</sup>-lacZ within 0-30

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min. after labeling when the labeling is performed in some exponentially growing yeast transformants (Fig. 7 and 9), does not reasonably provide enablement for assessing whether a cell with a functional 26S proteasome is quiescent or actively growing. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to a product and use of it for a method for assessing whether a cell with a functional 26S proteasome is quiescent or actively growing. The nature and breadth of the claimed invention encompasses using a DNA construct encoding for Ubl-reporter, wherein Ubl is any one of SEQ ID NO: 2-5 operably linked to any reporter, or any Ubl operably linked to reporter that is identified by claims 9 and 12 wherein said construct is transfected into a cell with a functional 26S proteasome.

The art of construction of DNA molecules encoding for fusion proteins is highly developed and skills of artisan high, however, because Applicants do not describe a functional 26S proteasome, and for that matter a cell with a functional 26S proteasome, one skilled in the art would not know which cell to choose, as comprising "functional 26S proteasome, for transfection and assessment of the state of growth. Whether a cell has the functional 26S proteasome is left to be determined by the one skilled in the art. This determination certainly involves an experimentation which is out of routine, taking into account the complexity of the 26 S proteasome structure and number of combination of mutations in the structure components that may/may not lead to degradation of the protein encoded by the claimed DNA construct.

The disclosure fails to provide guidance what a functional 26S proteasome is, and in result, experimentation left to those in the art has low probability of success and is improperly extensive and undue. Thus although Applicants by the last amendment limited the claimed DNA construct to those tested in *S. cerevisiae*, their data does not enable the invention as broadly claimed. Without further teachings on the part of Applicants as to the cells comprising functional 26S proteasome the experimentation imposed on the one skilled in the art is improperly extensive and undue.

### 3. Conclusion

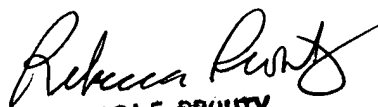
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All claims remain rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Malgorzata A. Walicka, Ph.D.  
Art Unit 1652  
Patent Examiner

  
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